AD 726206

TO: OFFICE OF NAVAL RESEARCH

FINAL PROJECT REPORT

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CONTRACT: Nonr 969 (03)

RATE: (variable)

CONTRACTOR: Research Foundation of State University of New York in behalf of State University of New York at Buffalo

PRINCIPAL INVESTIGATOR: E. H. Lanphier
Co-investigator: Hermann Rahn

Research Associates: J. N. Miller (1968-1970)
(others not supported by contract)

Assistants:
C. H. Smith, Jr. (1967-present)
E. A. Gard (1968-present)
J. F. Cunningham (1970-present)
W. J. Lawrence (1965-1966)
D. C. Marky (1970-present)
R. A. Morin (1959-1968)

TITLE OF PROJECT: High Pressure Physiology

Objectives:

(a) To investigate physiological problems arising from exposure to high pressures, as in an underwater environment;

(b) To make available a research training program for Submarine Medical Officers.

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SUMMARY OF RESULTS

a. Since start of project*:

The project was established in 1959, and work began when Mr. R. A. Morin and Dr. E. H. Lanphier arrived in August and September of that year. Planning, work on the compressed air system, and groundwork related to effects of gas density proceeded until delivery of the high pressure chamber in May of 1960. The chamber was put into operation almost immediately although completion of systems and of various kinds of instrumentation was a continuing process governed by funds, time and manpower, and the needs of ongoing research.

The first high pressure investigation concerned gas exchange during simulated breath-hold dives (1, 2, 45, 47). This was closely related to a field study of Rahn and Hong in the summer of 1960. The laboratory had also played a major role in preparations for that study. Interest aroused by these investigations led directly or indirectly to further work and to a number of additional publications from this laboratory (28, 37, 38) and elsewhere.

Physiological understanding of breath holding with air at normal pressure (2) and of breath-hold diving was markedly advanced. Hypoxia was identified as the cause of loss of consciousness and death in competitive breath-hold diving (1), and more evidence was advanced for decompression sickness as the cause of the "Taravana" syndrome (38).

An international symposium on breath-hold diving was held in Tokyo in 1965 at the time of the International Physiological Congress. This provided a forum for presentation of related work and for manifestation of the widespread interest awakened by this laboratory's concern with the subject. The proceedings were published in a 369-page volume (37).

From the outset, high pressure facilities were viewed as a major asset of physiological instrumentation and research capability. One of the implicit objectives was to apply them to a

* See also Annual Reports for 1960 through 1970.

wide variety of problems and to encourage the efforts and contributions of as many investigators of varied interests as possible. Over the years, this policy has enlisted a remarkable sum of interest, expertise, and manpower. The annual report of 1961 reflects the beginning of such cooperative relationships in a study of inert gas narcosis by Fenn, Snell, and Noell; work concerned with factors influencing development of atelectasis by Robertson (59); and O_2 and CO_2 toxicity studies of H. W. Gillen under another ONR contract.

A study of oxygen effects in the kidney by Rennie and Knox (6) foreshadowed a widespread growth of interest in the therapeutic potentialities and various problems of hyperbaric oxygenation. The Rennie-Knox study was, in fact, one of the first works to direct attention to potentially unfavorable vascular effects of oxygen.

As interest in hyperbaric oxygen (O_2 under high pressure, OHP) grew, our facility remained for a considerable time the only one available in a wide area for treatment or research. Clinical and research interests were accommodated wherever possible. They were reflected in a major animal study of OHP in treatment of myocardial infarction by Chardack et al. (5). A further examination of vascular effects of OHP by Hahnloser et al.(10) enlarged upon the findings of Rennie and Knox. Work by McSherry, Patterson, and Lanphier explored OHP and cerebral ischemia (9).

Our own persistent efforts to find a satisfactory measure of brain tissue oxygenation were never successful in terms of direct measurement, but our resulting familiarity with the problem led to interesting developments. A chance observation concerning the eye led to a study of OHP and persistence of vision in retinal ischemia by Carlisle, Lanphier, and Rahn (4, 50). This study had far-reaching effects in terms of our understanding of determinants of oxygenation (27) and the physiological basis of hyperbaric therapy (33). The same kind of interest later led to a major study of pulmonary O_2 toxicity with Winter from Harvard (11, 14, 55, 56).

The fact that we were among the very few physiologists with experience in high pressure involved a degree of responsibility in this field. This was fulfilled in part by starting a series of annual postgraduate courses in Hyperbaric Medicine, later sponsored by Dr. H. J. Alvis in his role of Director of Hyperbaric Medicine for the School of Medicine. Fulfilling the responsibility also entailed much committee service and much writing. Lanphier contributed over half of the text for the National Research Council book Fundamentals of Hyperbaric Medicine (33-36) and was called upon to contribute to various congresses and symposia (27, 29). Publications from this laboratory must have had a significant sobering influence both upon unwarranted enthusiasm and upon the tendency to disregard the hazards of hyperbaric medicine.

General familiarity with high pressure problems led to invitations to contribute chapters and articles to a number of publishers (24, 26, 30, 31, 32, 44). Some of these were major reviews which permitted summarizing past work of the laboratory, correlating this with the work of others, and helping to formulate future steps. Such was particularly true of a chapter on pulmonary function under high pressure contributed to the volume edited by Bennett and Elliott (44).

A basic interest of the laboratory from the outset concerned the influence of increased gas density on pulmonary ventilation. An early paper on this subject (3) reviewed Lanphier's observations at the Experimental Diving Unit in terms of subsequent work and study. Related interests were shared by others in the laboratory, including Maio and Farhi (12, 51), who conducted a major study of gas density and maximum voluntary ventilation (MVV) and related variables utilizing both the high-pressure and altitude facilities. Later work by Farhi's group at normal pressure clarified basic aspects of the problem of increased airway resistance during exercise (13).

A very early study came about largely in response to the contention by Bühlmann and Keller that nitrogen narcosis was in reality a manifestation of carbon dioxide retention, in turn related to increased work of breathing. Although incompletely reported in print (46, 49, 54), our observations became well known through meetings and personal contacts. We showed to our own satisfaction that narcosis occurred in the absence of CO_2 retention but could be accentuated markedly if arterial P_{CO_2} were elevated sufficiently by inadequate ventilation during exertion.

In 1962, the work of J. A. Kylstra in Leiden came to our attention. It concerned liquid breathing in mammals. This was of great interest not only because of the density of the breathing medium but also because of Rahn's longstanding interest in aquatic gas exchange (25). Kylstra was brought to Buffalo for two years, and definitive studies of liquid breathing were conducted in dogs. This work resulted in several publications (8, 39, 40, 52) and extraordinary gains of insight into airway behavior and intrapulmonary diffusion with a dense medium. The findings also contributed much to development of thoughts concerning interaction of limiting factors at depth (41), among which was a prediction of the hypoxic phenomena later encountered by Chouteau. Other work on distribution of ventilation with increased gas density by Cruz and Farhi (57) had not revealed problems of this sort. Closely related to the liquid breathing studies was work on artificial gills (43)by Paganelli and Bateman.

Continued liquid breathing studies with Schoenfisch were concentrated upon the mechanics of liquid breathing (61). The observations in that study in turn contributed to better understanding on our part of the phenomenon of dynamic airway compression on expiration described by Mead and his associates. This, in turn, made a major contribution to our approach to studies of ventilation with gas.

Active experimentation in the ventilatory field moved ahead with the arrival of Dr. J. N. Miller. His work confirmed the importance of expiratory airway compression in setting ventilatory limits of exertion at depth (15, 19, 23, 58). It also suggested that sustainable ventilation at depth might be equal to the MVV at depth. This in turn related to the concept that some addition of external expiratory resistance may be tolerable without reduction of ventilatory capacity.

An unsolved question also related to ventilation at depth is whether there is any respiratory depressant effect of nitrogen. The question is very difficult to attack directly because density is essentially inseparable from narcotic properties at depth. An indirect approach involved comparison of air with a mixture of nitrous oxide, oxygen, nitrogen, and helium that had the same density and P_{O_2} as air at normal pressure but produced a degree of narcosis like that of air at 300 ft. As a thesis project for the M.A. degree, Webber (60) conducted such comparisons at work and at rest. He discovered a singular increase of respiratory frequency with the narcotic mixture, but net ventilation appeared essentially unchanged.

The continuing interest of H. D. Van Liew in problems related to decompression, gas bubbles, and recompression led to a number of animal studies in which the high pressure facilities were used and significant information developed (7, 16, 53). Van Liew was able, for example, to provide detailed justification for the new USN treatment tables using oxygen at relatively low pressure.

New Facilities

Early 1967 saw the development and submission of a proposal for an unusual new laboratory of environmental physiology under Project Themis. This included a new high pressure chamber for pressures much beyond the existing capability. Since that time, a considerable proportion of time has been spent upon continued planning and development of this chamber and its systems and auxiliaries. The final product will be a vessel of 2500 psi working pressure with many unusual features (17, 18, 21) in keeping with the innovations of the laboratory as a whole (20, 22).

b. During current report period:

The arrival of CDR James Vorosmarti, MC, USN, in September 1970, marked the first time the second stated objective of this project had been fulfilled by actual presence of a Submarine/Diving Medical Officer. CDR Vorosmarti began as a candidate for the M.A. degree and took a number of formal courses during the Fall Semester. It was later possible to change his status to that of a postdoctoral fellow. This provides much greater freedom particularly for actual participation in research. CDR Vorsmarti's activities to date have included work with apparatus for respiratory measurements at depth, work with extensive data from earlier deep diving studies, and near-completion of preparations for the study of respiratory factors described below.

LCDR E. T. Flynn, Jr., MC, USN, will arrive in August of this year and will have the status of a postdoctoral fellow.

New facilities

The new chamber is expected to be hydro-tested at the Struthers-Wells plant in Warren, Penna., on 29 June 1971. Assuming that the test is successful, the only major work that will remain is completion of painting. Because of plant and laboratory vacations, installation may not occur before August. The chamber is now very much behind earlier schedules, but we have been in close touch with its progress and believe most of the delay was adequately explained by unforeseeable factors.

The pass-through locks with their unique outer doors have already passed hydrostatic test and appear to operate in accord with our best expectations. The main doors and 6-inch windows appear highly successful and will be tested with the vessel as a whole.

The air banks, bank manifold, "new" compressor, filter vessels, and the vast majority of high pressure piping have been installed. The chamber will be operable with compressed air almost as soon as it is in place. Completion of the wet/dry barriers will be one of the next-highest priority jobs.

Once operations on compressed air with wet/dry capability are established, the next priority concerns life-support equipment needed for closed-cycle He-O_2 operation. Five promising and innovative ideas for such equipment are the subject of a forthcoming proposal for developmental funds. A preliminary proposal was well-received. Two new approaches to lighting the chamber are close to completion of prototypes. Other adjuncts were described in the report of 1 May 1970, and further progress has been made with most of these.

Several papers concerning the new chamber have been presented and are slated to be published (17, 18, 21).

Factors modifying respiratory gas flow at depth

The main research undertaking in preparation recently and planned for coming months is the one with which CDR Vorosmarti is primarily concerned. The work of J. N. Miller in this laboratory (15, 19, 23) and of others elsewhere establishes the importance of dynamic compression of airways in modifying respiratory capacity at depth. Several interesting hypotheses arise from this insight. One was touched upon by Miller, when he cited evidence that at least with optimal breathing apparatus, maximum sustainable ventilation ($\dot{V}E_{max}$) in exercise at depth may be equal to the maximum voluntary ventilation (MVV) at the same depth.

A closely-related hypothesis is that some amount of external expiratory resistance may be tolerated without consequential reduction of expiratory flow rates, MVV, or $\dot{V}_{Emax}$. There is even some possibility of a beneficial effect from a small amount of such resistance. Accurate information in this area would be of great importance in the design and evaluation of underwater breathing apparatus.

The wet/dry capability of the new chamber will offer an unprecedented opportunity for the investigation of hydrostatic pressure differences as they affect a diver and his breathing equipment. A current hypothesis, related to those discussed above, is that a degree of "positive" bias may be beneficial. LCDR Flynn has a strong interest in this area of investigation.

Diffusion studies

Diffusion of gases through the pores of eggshell has proved to be a most useful model by means of which binary diffusion coefficients and the influence of ambient pressure can be investigated. The technique was initiated by Rahn and Wangensteen, and present studies under increased pressure are being carried out by H. K. Chang (School of Engineering) and D. Wilson. Departures of the system from theoretical predictions are of particular importance in improving ability to foresee the status of intrapulmonary diffusion under different conditions in deep diving. It appears more and more likely that "diffusion dead space" will be a major limiting factor in man's penetration of depth. Related studies are also being conducted elsewhere in the Department.

Pressure bradycardia

P. M. Hogan and E. H. Lanphier have conducted preliminary studies in dogs concerning pressure bradycardia. This is expected to become a major project during the coming year. The mechanism of heart-slowing at depth is not well-explained by gas partial pressures, and it is possible that this represents the first detectable evidence of a hydrostatic pressure effect on nerve or muscle. Intracellular microelectrode studies will be conducted if a systematic investigation of more central mechanisms fails to elucidate the phenomenon.

Other studies

Graduate students of Dr. Bishop are preparing for a study of hyperoxic effects upon peripheral neurological mechanisms. They will utilize a quantified approach to studying the Achilles tendon reflex and the "H" response in electrical stimulation of the nerve to the gastrocnemius muscle in man breathing O_2 at pressures to 2.8 ata.

J. V. Henderson, a graduate student/medical student who assists CDR Vorosmarti on a part-time basis, is spending the remainder of his time assembling instrumentation for intracellular microelectrode studies at increased pressure either in a manned chamber at moderate pressures or by remote operation in a small chamber for very high pressures. If his approach is successful, it will provide a very important capability.

Dr. Yair Cassuto, a postdoctoral fellow with Dr. Farhi, is about to begin pressure studies in rats and rabbits in which replacement of blood by fluorocarbon emulsions has been carried to a significant degree. The implications of such replacement are far-reaching in studies of gas transport.

PLANS FOR FUTURE

The highest priority for the immediate future under a new contract will be completion of the systems and adjuncts of the new facility. Work will proceed on projects outlined above and others that can be pursued in the existing chamber or with completed capability of the new one.

Larger-range plans assume that deep dives on closed-cycle He-O_2 will be possible. We hope to conduct both animal and human studies but believe our primary role will involve exposure of relatively large animals at exceptionally high pressures. (The maximum for the facility will be 171 atm abs.)

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